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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/718,534	11/24/2003	Jack D. Burton	330651	3647

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EXAMINER	
DUFFY, BRADLEY	

ART UNIT	PAPER NUMBER
1643	

DATE MAILED: 10/10/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/718,534	BURTON ET AL.	
	Examiner	Art Unit	
	Brad Duffy	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 September 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-38* is/are pending in the application.

4a) Of the above claim(s) *4,5,8-10,12-19 and 22-38* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,6,7,11,20 and 21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/25/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The amendment filed September 1, 2006 has been entered in full.

Election/Restrictions

2. Applicant's election with traverse of Group V claims 1-3, 6-7, 11, 20 and 21 in the reply filed on September 1, 2006 is acknowledged. The traversal is on the grounds that, "groups I, II, III, IV, V, VI and XXIII are all classified in the same class, 530 and subclass 388.85", and that "the Examiner would not be seriously burdened if this restriction was not made." However, this is not found persuasive. Applicant has provided no evidence to establish why the requirement for restriction is improper. Upon reconsideration, Groups I-III should be placed in class 530, subclass 387.7, 387.9 or 388.85, for example, as they are drawn to antibodies targeting the CEA antigen and the antibodies targeting HLA-DR in Groups IV-VI and XXIII should be placed in class 530, subclass 388.7, 388.73 or 388.75, for example. Furthermore, classification of subject matter is merely one indication of the burdensome nature of the search involved. In this case, the literature search is particularly relevant in this art and would not be co-extensive. Therefore, the literature search is much more important in evaluating the burden of search. Clearly different searches and issues are raised in the examination of each group, which would create a burden on the Office. For these reasons the restriction requirement is deemed to be proper and is made FINAL.

3. Claims 4-5, 8-10, 12-19 and 22-38 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim.

4. Claims 1-3, 6-7, 11, 20 and 21 are under examination to the extent that the targeting moiety comprises a conjugate of an antibody specific to HLA-DR and the ligand-binding region of interleukin-4 receptor α.

Specification

5. The abstract of the disclosure is objected to because of the following informalities:

In the second sentence the word "a" should be removed, where it precedes "an antibody".

6. The disclosure is objected to because of the following informalities:

In the first sentence, the status of Application 09/231642 needs to be updated to indicate that it is now U.S. Patent 6,703,488.

Appropriate correction is required.

Claim Objections

7. Claims 1-3, 6-7, 20 and 21 are objected to as being drawn to non-elected embodiments.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 1-3, 6-7, 11, 20 and 21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

10. Claims 1-3, 6-7, 11, 20 and 21 are indefinite for reciting "linked", in claim 1. Are the antibody and ligand-binding region covalently linked, linked by the fact that they are in the same solution, linked by being bound to each other, or linked in some other manner? Futhermore, if they are covalently linked, is it a peptide linkage creating a fusion polypeptide, a chemical linkage between specific amino acids of the antibody and the ligand-binding region, a chemical linkage between random amino acids of the antibody and the ligand-binding region or some other covalent linkage and is there a linker between the antibody and ligand-binding region? Finally, if the antibody and the ligand-binding region are linked as a fusion polypeptide, is the antibody or the ligand-binding region N-terminal to the other and is there a linker polypeptide between the two? Accordingly, the claim is indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

11. Claims 6 and 11 are indefinite for reciting the abbreviation "HLA-DR". Full terminology should be used in the first instance in the claims, followed by the abbreviation in parentheses. Dependant claims may then use the abbreviation.

Abbreviations render claims indefinite because the same abbreviation may represent more than one element or concept.

Claim Rejections - 35 USC § 103

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

13. Claims 1-3, 6-7, 11, 20 and 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hu et al (Cancer Research 56:4998-5004, November 1, 1996), in view of Galizzi et al (JBC 264(12):6984-6989, April 25 1989).

The claims are drawn to a targeting moiety comprising a conjugate of an antibody specific to HLA-DR linked to the ligand-binding region of interleukin-4 receptor α and a composition comprising said targeting moiety and a pharmaceutically acceptable carrier.

Hu et al teach a targeting moiety comprising a fusion protein of the Lym-1 antibody (see page 17, line 9 of the specification that discloses the Lym-1 antibody is directed against an HLA-DR epitope) to interleukin 2 (see abstract). Furthermore, Hu et al teach the Lym-1/IL-2 fusion protein in a composition comprising a pharmaceutically acceptable carrier as this protein was injected into mice (see page 5001, second column and 5002, first column). Finally, Hu et al teach that the Lym-1/IL-2 fusion protein was constructed to increase the permeability or internalization of the Lym-1 antibody to treat malignant lymphomas and that such a fusion increased the cytotoxicity of the Lym-1 antibody by at least 2-fold (see page 4998, second column and abstract) in Raji cells (Raji cells are a cell line derived from Burkitt's lymphoma—see definition from The Dictionary of Cell and Molecular Biology-Online, http://www.mblab.gla.ac.uk/~julian/dict2.cgi?5532, viewed 9/27/2006). Hu et al do not

teach a HLA-DR antibody fused to the ligand-binding region of IL-4 receptor α or a composition comprising the HLA-DR antibody linked to IL-R α and a pharmaceutically acceptable carrier. This deficiency is made up for in the teachings of Galizzi et al.

Galizzi et al teach that the ligand-binding region of the IL-4 receptor α and IL-4 are components of a rapidly internalized receptor system wherein 80% of receptor-bound IL-4 is internalized within 20 minutes from the Burkitt's lymphoma cell line Jijoye (see abstract, page 6984, second column and 6985, first column and 6986, second column). It should be noted here that the IL-4 receptor α is a subunit of the IL-4 receptor mentioned in Galizzi and that the IL-4 receptor α subunit is the ligand-binding region of the IL-4 receptor, so it necessarily would be internalized with the IL-4 receptor and IL-4.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to fuse the ligand-binding region of IL-4 receptor α to the Lym-1 antibody of Hu and produce it in a composition with a pharmaceutically acceptable carrier for therapeutic benefit in treating lymphoma patients.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success at the time the invention was made to fuse the ligand-binding region of IL-4 receptor α to the Lym-1 antibody of Hu and produce it in a composition with a pharmaceutically acceptable carrier for therapeutic benefit in treating lymphoma patients because Hu et al teach that Lym-1 antibodies are poorly internalized and that a component of a rapidly internalized receptor system (in this case IL-2) can increase internalization of Lym-1 antibodies and cytotoxicity in a lymphoma cell line (see

table 2 and abstract) and Galizzi et al teach that the IL-4 receptor α is a component of a rapidly internalized receptor system in a lymphoma cell line (see abstract). Therefore, one of ordinary skill in the art at the time the invention was made would have been motivated to fuse the ligand-binding region of IL-4 receptor α to the Lym-1 antibody of Hu and produce it in a composition with a pharmaceutically acceptable carrier to increase the internalization of the Lym-1 antibody into lymphoma cells. Furthermore, one of skill in the art would have had a reasonable expectation of success, because it was well known that components of a rapidly internalizing receptor system increase the internalization of Lym-1 antibodies as taught by Hu et al and that the IL-4 receptor was a component of a rapidly internalizing receptor system as taught by Galizzi. Thus, there would be an advantage and a reasonable expectation of success in using the ligand-binding region of IL-4 receptor α fused to the Lym-1 antibody in lymphoma patients expressing HLA-DR and it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to fuse the ligand-binding region of IL-4 receptor α to the Lym-1 antibody and produce it in a composition with a pharmaceutically acceptable carrier to facilitate the administration, in view of Hu et al and Galizzi et al.

Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

Double Patenting

14. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent

and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

15. Claims 1-3, 6-7, 11, 20 and 21 are provisionally rejected on the grounds of nonstatutory obviousness-type double patenting as being unpatentable over claims 15-16, 20 and 30 of copending Application No. 11/368,296, in view of Galizzi et al (JBC 264(12):6984-6989, April 25 1989) and Hu et al (Cancer Research 56:4998-5004, November 1, 1996). Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims only differ slightly in scope.

The instant claims have been described *supra*.

Claims 15-16, 20 and 30 of copending Application No. 11/368,296 are drawn to an HLA-DR antibody conjugated to a peptide in a pharmaceutical composition. The claims in copending Application No. 11/368,296 do not teach that the peptide conjugated to the HLA-DR antibody is IL-4 receptor α. These deficiencies are made up for in the teachings of Galizzi et al and Hu et al.

Galizzi et al has been described *supra.*

Hu et al has been described *supra.*

The claims in the instant application are obvious variants of claims 15-16, 20 and 30 of copending Application No. 11/368,296 because it would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to conjugate the ligand-binding region of IL-4 receptor α to the HLA-DR antibody of copending Application No. 11/368,296 and produce it in a composition with a pharmaceutically acceptable carrier for therapeutic benefit in treating lymphoma patients.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success at the time the invention was made to conjugate the ligand-binding region of IL-4 receptor α to the HLA-DR antibody of copending Application No. 11/368,296 and produce it in a composition with a pharmaceutically acceptable carrier for therapeutic benefit in treating lymphoma patients in view of Galizzi et al and Hu et al, because Galizzi et al teach that the IL-4 receptor α is a component of a rapidly internalized receptor system in a lymphoma cell line (see abstract and Figure 7) and Hu et al teach that a component of a rapidly internalizing receptor system (IL-2) increase the internalization of Lym-1 antibodies (recognize HLA-DR epitope) in a lymphoma cell line (see table 2 and abstract). Therefore, one of ordinary skill in the art at the time the invention was made would have been motivated to fuse the ligand-binding region of IL-4 receptor α to the HLA-DR antibody of copending Application No. 11/368,296 and produce it in a composition with a pharmaceutically acceptable carrier

to increase the internalization of the HLA-DR antibody of copending Application No. 11/368,296 into lymphoma cells. Furthermore, one of skill in the art would have had a reasonable expectation of success, because it was well known that components of a rapidly internalizing receptor system increase the internalization of Lym-1 antibodies (recognize HLA-DR epitope) as taught by Hu and that the IL-4 receptor was a component of a rapidly internalizing receptor system as taught by Galizzi. Thus, there would be an advantage and a reasonable expectation of success in using the ligand-binding region of IL-4 receptor α conjugated to the HLA-DR antibody of copending Application No. 11/368,296 in lymphoma patients expressing HLA-DR and it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to fuse the ligand-binding region of IL-4 receptor α to the HLA-DR antibody of copending Application No. 11/368,296 and produce it in a composition with a pharmaceutically acceptable carrier to facilitate the administration, in view claims 15-16, 20 and 30 of copending Application No. 11/368,296 and Galizzi et al and Hu et al.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

16. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

US Patent 5,59905, Mosley et al, 102(e) date: at least February 14, 1990.

US Patent 6,210,661, Enssle et al, 102(e) date: August 27, 1993.

US Patent 6,328,954, Enssle et al, 102(e) date: August 27, 1993.

Baier et al. Journal of Virology, 69(4):2357-2365, April 1995.

DeNardo et al. Int. J. Cancer, Supplement 3:96-101, 1988.

Debinski et al. JBC, 268(19):14065-14070, July 5, 1993.

17. No claims are allowed.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brad Duffy whose telephone number is (571) 272-9935. The examiner can normally be reached on Monday through Friday 7:00 AM to 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Respectfully,
Brad Duffy
571-272-9935

David Blanchard
AU 1643